Remarks

Claims 1-6, 9-12 and 24-34 remain pending in the application, with claims 1, 6, 27 and 31 being the independent claims. Claims 1-3, 5, 25-27 and 31 have been amended. These amendments are believed to introduce no new matter.

Support for the amendments to claims can be found throughout the specification. For example, support for the amendments to claims 1 and 31 can be found in claim 20 as originally filed as well as at page 5, lines 24 to 26. Support for the amendment to claims 3 and 27 is found, for example, at page 13, lines 4 to 14. Support for the amendments to claims 5 and 25, can be found, for example, at page 45 between lines 17 and 19.

Applicants thank the Examiner for the withdrawal of the rejection of claim 3 under 35 U.S.C. § 112, second paragraph and for the allowance of claims 6 and 9.

Specification

The Office has objected to the disclosure "because it contains an embedded hyperlink and/or other form of browser-executable code at page 25 line 27" (OA at p. 3). Applicants respectfully believe that the Office mistakenly referred to page 25 of the specification, whereas the hyperlink appears at pages 28, 33 and 49. Accordingly, Applicants respectfully submit that the objections to the specification have been overcome by the replacement of the embedded hyperlink at pages 28, 33 and 49 by its corresponding paper reference. Further, insertion of references to the sequence identifiers in the legend for Figure 5 (the formal drawings will include the sequence identifiers) overcomes the Office's objection to the specification. Accordingly, withdrawal of the objections to the specification is respectfully requested.

Rejections Under 35 U.S.C. § 112, second paragraph

The rejection of claims 3 and 25-30 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite is respectfully traversed. Applicants note that the Office originally stated that claims 3 and 26-30 were rejected under 35 U.S.C. § 112, second paragraph (OA at p. 3). However, later in the OA at page 4, claim 25 was rejected for lack of antecedent basis. Therefore, Applicants address the rejection to claim 25 below.

Claims 3 and 27 have been amended to explicitly insert a recitation of high stringency conditions. Accordingly, withdrawal of the rejection of these claims as indefinite is respectfully requested.

Likewise, claim 25 has been amended to recite "a predicted open reading frame." Thus, it is respectfully requested that withdrawal of the rejection regarding antecedent basis be withdrawn.

Claim 26 now recites "consists of the sequence set forth in SEQ ID NO: 4," thus clarifying the metes and bounds of the invention.

Accordingly, reconsideration and withdrawal of the rejection of claims 3, 25-30 under 35 U.S.C. § 112, second paragraph, is respectfully requested. The preceding amendments have been made solely to expedite prosecution and should not be taken as acquiescence to the Office's rejections.

Rejections Under 35 U.S.C. § 112, first paragraph

The rejection of claims 1-5, 10-12, 24, 25 and 27-34 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement is respectfully traversed.

Claims 1-2, 10-12 and 25

In the first aspect of the rejection under 35 U.S.C. § 112, first paragraph, claims 1-2, 10-12 and 25 are rejected. The Office argues that "the Office could not envision how [sic] the claimed structure(s) looks like or what the function of the claimed nucleic acid molecule(s) is" and that "[t]here is not even identification of any particular structure or function in the claims" (OA at pp. 5-6). Applicants respectfully

submit that the claimed subject matter has been sufficiently characterized not only in terms of its function but also in terms of its structure.

Specifically, the claimed isolated nucleic acid molecule is characterized in terms of its structure (*i.e.*, the isolated nucleic acid molecule contains additional sequence between exon 3 and exon 4a), and by the relationship between its structure and its function (*i.e.*, the additional nucleic acid sequence indicates that the isolated nucleic acid molecule is a differentially expressed prostate cancer antigen 3 (PCA3) mRNA indicative of a non-malignant state of the prostate). Thus, the claimed molecules have been characterized by structure, function and the relationship between structure and function. As such, one of skill in the art would recognize that the inventors were in possession of the claimed, fully characterized invention as of the filing date. *See The Regents of the University of California v. Eli Lilly and Company*, 119 F.3d 1559, 1569 (Fed. Cir. 1997) ("[a] description of a genus of [nucleic acid molecules] may be achieved by . . . a recitation of structural features common to all members of the genus, which features constitute a substantial portion of the genus.").

Claims 1-2, 5, 10-12, 25 and 27-34

In the second aspect of the rejection under 35 U.S.C. § 112, first paragraph, claims 1-2, 5, 10-12, 25 and 27-34 are rejected. The Office argues that the protein sequence of PCA3 is not sufficiently described in the specification. First, Applicants respectfully submit that claims 5 and 25 refer to the encoded PCA3 protein. As now presented these claims recite "predicted open reading frame encoding...". Therefore, it is submitted that claims 5 and 25 clearly define the characteristic features of the claimed nucleic acid sequence encoding the predicted PCA3 protein.

Moreover, the specification of the above-identified application conveys to the skilled artisan that the inventors were in possession of the nucleotides claimed in claims 5 and 25. The disclosure of each species of a claimed genus is not required in order to show possession of the genus. *Utter v. Hiraga*, 845 F.2d 993, 998 (Fed. Cir. 1988). Rather, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. MPEP § 2163.05. In fact, the courts have found possession of a genus with the disclosure of only one species. *Id.* In the present application, the nucleotides claimed in claims 5

and 25, *i.e.*, those that are predicted to encode a defined amino acid sequence, are a well-defined genus. One skilled in the art would know that a finite number of nucleotides are present in the claimed genus and would recognize each species of the claimed genus. Accordingly, one of skill in the art would recognize that the inventors possessed such a genus as of the filing date.

The Office has further stated that "claims 27 and 31 recite 'complementary' sequence and the dependent claims 28 and 32 says the complementary sequences are used to make recombinant nucleic acid with a promoter such initiation of transcription occurs" (OA at p. 6). The Office further states that human complementary sequences usually do not encode any protein except in rare instances and the specification does not teach that complementary sequences encode any peptide. *Id.*

Applicants wish to point out that dependent claims 28 and 32 do not require that the claimed sequences be complementary sequences. Claim 28 narrows independent claim 27, and claims a subset of nucleic acid molecules in claim 27. Claim 28 does not necessarily dictate that the claimed nucleic acid molecules are complementary sequences.

Likewise, claim 32 narrows independent claim 31, and claims a subset of nucleic acid molecules in claim 31. Claim 31 does not necessarily dictate that the claimed nucleic acid molecules are complementary sequences.

Further, the Office alleges that the "[o]ther problems in the claims are hybridizing nucleic acid molecules. The specification does not describe what kind [of] activity is associated with the genus of nucleic acid molecules being claimed" (OA at p. 6). Applicants reiterate that the claims recite that the long PCA3 mRNA is indicative of a non-malignant state of the prostate. The specification supports this limitation in the claims:

> [t]he RNA lacking the additional sequence is associated with prostate cancer whereas the RNA comprising same is associated with a non-malignant prostatic state.

Specification at p. 5, lines 24-26. Therefore, the specification does state the activity of the claimed nucleic acid molecules.

Claims 1, 3-4, 27 and 31

In the third aspect of the rejections under 35 U.S.C. 112, first paragraph, claims 1, 3-4, 27 and 31 are rejected. The Office alleges that "[t]he specification at Figure[] 3 teaches that instant SEQ ID NO:1 is not an entire open reading frame but a PCR-amplified partial sequence from between two exons of a known gene" and further that the "specification does not teach what the entire open reading frame that includes 27 to 254 nucleotide of SEQ ID NO:1 [sic]" (OA at p. 7).

The Office appears to be implying that claim 1 is directed to a partial sequence of an entire open reading frame. This is in error. None of rejected claims 1, 3-4, 27 and 31 recite that the claimed nucleic acid molecule encodes a PCA3 protein and/or contains a putative open reading frame. The insert between exon 3 and 4a increases the size of the PCA3 mRNA or nucleic acid, thereby yielding a longer PCA3 nucleic acid sequence which is associated with a non-malignant state of the prostate. To reiterate, no protein sequence is claimed, except in claims 5 and 25, which while relating to a purified nucleic acid sequence, characterize a predicted protein encoded by the nucleic acid sequence.

Unlike an EST, the claimed sequence has been fully characterized and its significance has been determined by the present inventors. Taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the applicant was in possession of the genus of nucleic acid sequences that comprise, for example, nucleotides 27 to 254 of SEQ ID NO:1 (the additional sequence).

The Office has cited *Vas-Cath Inc. v. Mahurkar* and alleges that "only SEQ ID NO: 1, but not the full breath of the claim meets the written description provision" (OA at p. 7). In addition, the Office argues that "definition by function alone does not suffice, to sufficiently describe a coding sequence 'because it is only an indication of what the gene does, rather than what it is'" (OA at p. 8, citation omitted). Applicants respectfully submit that claim 1 meets the written description requirement because the nucleic acid molecule of claim 1 is characterized in terms of its structure and its function. Specifically, amended claim 1 introduces not only functional language (non-malignant) but also structural characteristics, *e.g.*, the fact that the sequence is longer than SEQ ID NO 2, and the fact that the insertion is between exon 3 and exon

4. Accordingly, distinguishing features of the claimed nucleic acid sequences are explicitly present in the claims.

Applicants stress that while the name PCA3 refers to prostate cancer antigen, it should not be interpreted as always encoding a polypeptide. Of note, the predicted ORF found in PCA3 nucleic acid sequence only covers 153 nucleotides (51 amino acids) out of a possible approximately 3,600 nucleotides. The putative amino acid encoding aspect of the PCA3 nucleic acid sequence is but one aspect of the different features of the PCA3 nucleic acid sequences of the present invention. The set of claims now pending focus on the nucleic acid sequences of PCA3, and more particularly on the fact that an insert between exons 3 and 4a yields a longer PCA3 nucleic acid sequence which is not associated with a malignancy of prostate cancer.

In view of the above and foregoing, Applicants request that the Office withdraw the rejection of claims 1-5, 10-12, 24, 25 and 27-34 under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. § 102

The previously indicated allowability of claims 1-2, 4-5, 24-25 and 27 has been "withdrawn in view of the newly discovered reference(s) to Bussemakers et al (AT2 of IDS filed on 11/12/2003, 1993, Urol. Res. 21: 452, Abstract No.P42, Springer International)" (OA at p. 8). The rejection of claims 1-5, 24-25, 27 and 31 under 35 U.S.C. § 102(b) as allegedly being anticipated by Bussemakers *et al.*, *Urol. Res. 21*:452, Abstract No. P42, Springer Int'l. (1993) ("Bussemakers I") as evidenced by Bussemakers *et al.*, *Cancer Res. 59*:5975-5979 (1999) ("Bussemakers II") and "Figs. [sic] 3 of the instant specification" is respectfully traversed.

The Office has not demonstrated that Bussemakers I discloses each and every limitation of claim 1. Such a demonstration is necessary to prove anticipation. Claim 1 recites an isolated nucleic acid molecule encoding a differentially expressed prostate cancer antigen 3 (PCA3) mRNA, wherein said isolated nucleic acid molecule contains additional sequence between exon 3 and exon 4a, thereby encoding a PCA3 mRNA having a sequence which is longer than that set forth in SEQ ID NO:2, wherein said longer isolated nucleic acid is indicative of a non-malignant state of the prostate. Bussemakers I does not disclose or suggest the sequence of its disclosed

transcripts, and does not teach the presence of "exon 3" or "exon 4a," or the presence of additional sequence between those exons.

Further, claims 1 and 31 recite that the longer PCA3 mRNA (or of the sequence between nucleotides 27 to 254 of SEQ ID NO:1) indicates a non-malignant state of the prostate, while the Bussemakers citations fail to teach (1) such PCA3 sequences (*i.e.*, associated with a non-malignant state), and (2) an insert between exons 3 and 4a, or (3) the sequence between nucleotides 27 to 254 of SEQ ID NO:1. It is therefore submitted that Bussemakers references fail to anticipate claims 1 or 31.

In addition, even assuming for the sake of argument that the transcripts disclosed in Bussemakers I are encompassed by one or more of the present claims, Bussemakers I does not contain an enabling disclosure. For a reference to be available as prior art under 35 U.S.C. § 102(b), the reference must enable the claimed invention. Bussemakers I is a mere twenty six line abstract that does not enable one of skill in the art to practice the claimed invention, *i.e.*, to make or use the nucleic acid molecule according to claim 1. Bussemakers I discloses the identification of "[t]welve apparently differentially expressed mRNAs (overexpressed in tumor or in normal tissue) were identified in this way. The complementary DNA fragments were recovered from gel, reamplified and used as probes for Northern analysis. One of the probes (DD3) detected two transcripts . . ." (Bussemakers I at p. 452). Bussemakers I does not disclose experimental details sufficient to further characterize the disclosed RNAs and does not disclose the sequence of the transcripts.

With respect to independent claim 27, it is respectfully submitted that (1) since neither Bussemakers references teach a sequence which comprises the sequence between positions 27 and 254 of SEQ ID NO:1, this sequence has not been identified prior to the present invention, and (2) since claim 27 has been amended to delete the "open language", that the rejection of claim 27 over either of the Bussemakers references has also been overcome.

It follows that all claims dependent on claims 1, 27 or 31 also overcome the rejection for anticipation over the two Bussemakers citations.

The rejection of claims 1-3, 5 and 10-12 set forth in the first substantive Office Action (January 11, 2002) has also been reinstated. The rejection of claims 1-5, 10-12 and 24-34 as allegedly anticipated under 35 U.S.C. § 102(a) by Bussemakers Int'l. Appl. No. WO 98/45420 ("Bussemakers III") is respectfully traversed.

Bussemakers III does not anticipate the present claims. Specifically, the Office argues that "[c]laims 1, 2, and 25 read on any nucleic acid longer than SEQ ID NO:2 (278 nucleotides) because the claims do not specify any structure of the claimed nucleic acid molecule(s) and does not specify any function of the claimed nucleic acid, either" (OA at p. 10). As discussed in detail above, both the structure and the function of the nucleic acid molecules in claims 1, 2 and 25 are explicitly disclosed in the claims.

Further, Bussemakers III does not teach a PCA 3 nucleic acid sequence indicative of a non-malignant state of the prostate.

In addition, Bussemakers III does not anticipate any one of claims 1-5, 10-12 and 24-34 because Bussemakers III does NOT teach the 27 to 254 nucleotide sequence of SEQ ID NO:1. Applicants stress that contrary to the Examiner's interpretation that "[i]t appears that instant SEQ ID NO:1 lies between ex[o]n 3 and 4a of the PCA3 transcription unit" (OA at p. 12), the exemplified sequence which lies between exon 3 and 4a is the sequence spanning nucleotides 27-254 of SEQ ID NO:1.

In view of the above and foregoing, Applicants respectfully request that the Office withdraw the rejections under 35 U.S.C. § 102(b) and 35 U.S.C. § 102(a).

Conclusion

Prompt and favorable consideration of this Amendment is respectfully requested. Applicants believe the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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